Composition comprising lignin and antidi arrheal component

Jacobsen, Gunner; Munk, Jens Kristian

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(71) Applicant *(for all designated States except US)*: **Biofiber-Damino A/S** [DK/DK]; Staushedevejen 10, DK-6621 Gesten (DK).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **JACOBSEN, Gunner** [DK/DK]; Troelsevej 280, DK-5491 Blommenslyst (DK). **VILLADSEN, Jens, Kristian, Munk** [DK/DK]; Kallerupvej 149, DK-5230 Odense M (DK).

(74) Agent: **Plougmann & Vingtoft a/s**; Sundkrogsgade 9, Post Office Box 831, DK-2100 Copenhagen Ø (DK).

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(54) Title: COMPOSITION COMPRISING LIGNIN AND ANTIDI ARRHEAL COMPONENT

(57) Abstract: The present invention relates to a composition comprising lignin and at least one compound selected from the group consisting of bromelain, papain, tannin, carvacrol, thymol, alliin, allicin, fenugreek seed, egg, poppy, poppy seeds, humic acid, roots, kaolin, catechu, cellulase, flavonoid and isphagula husk. In particular it relates to the use of said composition as a food, feed, and/or food- or feed supplement. Additionally it relates to the method of preparing the composition.

COMPOSITION COMPRISING LIGNIN AND ANTIDIARRHEAL COMPONENT

Technical field of the invention

The present invention relates to a composition comprising lignin and at least one compound selected from the group consisting of bromelain, papain, tannin , carvacrol, thymol, alliin, allicin, fenugreek seed, egg, poppy, poppy seeds, humic acid, roots, kaolin, catechu, cellulase, flavonoid and isphagula husk. In particular it relates to the use of said composition as a food, feed, and/or food- or feed supplement. Additionally it relates to the method of preparing the composition.

Background of the invention

When rearing farm animals a serious problem is the fact that a large percentage of animals are infected with enteric pathogens. When the animal is infected with enterotoxics such as bacterias (e.g. Escherichia Coli) or a virus in the gastrointestinal tract, the toxin binds to specific receptors on the surface of cells lining the gut, this binding induces the cell to open a pore through which the toxin is transported or the toxin binds on the cell surface and the entire structure is internalized. The cells thus affected by the toxin are then unable to properly control the fluid balance within the intestine. Fluid is not adequately absorbed by the gut lining resulting in fluid overload of the intestine. These excess fluids result in a massive increase in the water content of faeces and the very liquid manure associated with diarrhoea or "scours". This may result in a decreased weight gain of the infected animal having diarrhoea or in worst case that the animal gets weak and dies.

Therefore there is a continuing need for a composition which may treat or prevent diarrhoea caused by a gastrointestinal disorder.

EP 0 820 306 B1 relates to a pharmaceutical agent comprising a mixture of a pectinaceous plant fibre material with a phospholipid. The agent is used for treating disorders associated with the alimentary tract such as diarrhoea or gastric ulcers in animals and humans.

WO 2004/043451 A1 discloses a composition comprising isphagula husk, amino acid and at least one carbohydrate and electrolyte. The composition is used as a therapeutic agent, such as for use in treating disorder in the intestinal system of monogastric animals.

WO 99/62355 A1 discloses a piglet feeding method comprising administration to the piglet at least during the entire suckling period two different feed supplement compositions

comprising dietary fibres, iron and other micronutrients including copper and zinc, where the first composition has the highest content of iron. WO 99/62355 A1 discloses a third feed supplement composition comprising dietary fibres and electrolytes may be used to prevent or cure diarrhoea as a substitute for antibiotic treatment.

Summary of the invention

In one aspect the present invention relates to a composition comprising lignin and at least one compound selected from the group consisting of bromelain, papain, tannin, carvacrol, thymol, alliin, allicin, fenugreek seed, egg, poppy, poppy seeds, humic acid, roots, kaolin, catechu, cellulase, flavonoid and isphagula husk.

In another aspect the invention relates to a method of preparing said composition by mixing the components comprised in the composition.

In another aspect the present invention relates to a composition of the invention for the use as a medicament.

In another aspect of the invention it relates the use of the composition for the manufacture of a medicament for treating diarrhoea.

Another aspect relates to the use of the composition as food, feed or a supplement for humans, pigs, cattle, sheep, goats, horses, chickens, turkeys, pigeons, camels, llamas, dogs and cats.

Another aspect of the invention relates to the administration of the composition in the range of from 1-3000 mg/kg body weight/day of treatment.

Another aspect of the invention relates to a method of treating diarrhoea in animals or humans comprising administration of a composition.

Detailed description of the invention

Definitions

Prior to discussing the present invention in further details the following terms and conventions will first be defined:

In the context of the present invention the reference to "w/w%" is to be, unless otherwise stated, calculated on the basis of the content of solids, i.e. as the weight percentage of the content of dry matter. In this context the term "dry matter" refers to the solids in a composition which are present after evaporation of any free water. In some instances there may be referred to a composition comprising one or more components, wherein the sum of said components is less than 100 w/w%. This means that the composition may comprise other components than those specified in that particular context.

The composition of the present invention comprises lignin in combination with one or more compound selected from the group consisting of bromelain, papain, tannin, carvacrol, thymol, alliin, allicin, fenugreek seed, egg, poppy, poppy seeds, humic acid, roots, kaolin, catechu, cellulase, flavonoid and isphagula husk. The inventors of the present invention have observed that administration of such compounds to piglets increased the weight of these animals. Without being bound by any theory the inventors believe that this effect on weight gain is caused by lignin in combination with any one of the compounds, bromelain, papain, tannin, carvacrol, thymol, alliin, allicin, fenugreek seed, egg, poppy, poppy seeds, humic acid, roots, kaolin, catechu, cellulase, flavonoid and isphagula husk having an anti-diarrhoeal, anti-viral, anti-bacterial or any combination of the three effect on animals. Diarrhoea is a gastrointestinal disorder which in many instances is caused by a pathogenic infection. By the term "compound with anti-diarrhoeal effect" is hereby meant a compound which has a beneficial effect on the gastrointestinal tract, such that diarrhoea is minimized. Without being bound by any theory the inventors believe that any composition of the present invention may have an antidiarrhoetic, anti-viral, anti-bacterial or any combination of the three on the entire gastrointestinal tract, particularly the intestine or jejunal intestine, or any composition of the present invention may act by regulating the balance of salt and/or glucose or by regulating the microbial balance of the intestine. The anti-diarrhoeal effect can be measured as an increased weight gain of humans or animals fed with the compound, e.g. piglets, compared to humans or animals fed with a control diet without the compound. This may for example be measured as shown in the example. Additionally a decreased mortality of animals can be detected in such animals fed the compound compared to control.

Composition of the present invention

The composition of the present invention comprises lignin and at least one compound selected from the group consisting of bromelain, papain, tannin, carvacrol, thymol, alliin, allicin, fenugreek seed, egg, poppy, poppy seeds, humic acid, roots, kaolin, catechu, cellulase, flavonoid and isphagula husk. Optionally, the composition comprises further components.

The composition may be used for different purposes such as a food, feed, or food- or feed supplement, and the choice and amount of further components vary thereof. For example if the composition is used as a food or feed it will likely comprise ingredients which are necessary in a typically diet such as fat, protein, carbohydrate, vitamins, or minerals. However if the composition is used as a feed supplement it may include fewer components than the food or feed. The components comprised in the feed supplement may be nutritious compounds such as herbs, electrolytes, minerals or vitamins. The food- or feed supplement may be used either in solid form by sprinkling onto conventional animal feed or by injecting it in a fluid form into the mouth of an animal.

Lignin

As previously described the present invention relates to a composition comprising lignin and at least one compound selected from the group consisting of bromelain, papain, tannin, carvacrol, thymol, alliin, allicin, fenugreek seed, egg, poppy, poppy seeds, humic acid, roots, kaolin, catechu, cellulase, flavonoid and isphagula husk.

The inventors of the present invention believe that feeding animals with lignin, in particular farm animals such as pigs, cattle, sheep, goats, horses, chickens, turkeys, pigeons, camels, llamas, or domestic animals such as dogs and cats, gives beneficial effects on the gastrointestinal tract and thus prevent and/or decrease the severity of diarrhoea.

Lignin is a large and complex macromolecule which consists of various types of substructures which repeat in random manner. Lignin has a molecular mass in excess of 10.000 amu (atomic mass unit) and is hydrophobic and aromatic in nature. Lignin is comprised by 3 different phenylpropanoids (C6-C3), also termed monolignols; coniferyl alcohol, sinapyl alcohol and *p*-coumaryl alcohol. Different plants use different ratio of monolignols, for example lignin in grasses is almost entirely *p*-coumaryl alcohol.

The composition of the present invention can comprise any sort of lignin, both low-molecular lignin and high molecular lignin and can comprise different amounts of the monolignols, coniferyl alcohol, sinapyl alcohol and *p*-coumaryl alcohol.

Lignin is most commonly derived from wood and it is an integral part of the cell walls of plants. Lignin fills the spaces in the cell wall between cellulose, hemicellulose and pectin components. Lignin is difficult to degrade and is therefore an efficient barrier against pathogens which would invade plant tissue. Furthermore lignin is difficult to degrade in the gastrointestinal system of humans and animals.

In farm animal production diarrhoea in young animals is a serious problem which is presently prevented or treated by the use of antibiotics. The inventors of the present invention believe that lignin is able to increase the growth rate and/or survival of animals or humans which is believed to be caused by that lignin has a beneficial effect on the gastrointestinal tract of the animal such that incidences of diarrhoea are lowered.

In an embodiment of the present invention the composition used as a feed supplement comprises at least 0.01%w/w lignin, such as in the range of 0.01-30w/w% lignin, or in particular in the range of 0.5-20 w/w%, or in the range of 1-15 w/w%, or in the range of 2-15 w/w%, or in the range of 1-10w/w%, or in the range of 2-10 w/w%, or in the range of 2.5-10 w/w%, or in the range of 3-10 w/w%, or in the range of 1-8 w/w%, or in the range of 2-7 w/w%.

In another embodiment of the invention, the composition used as a food or feed comprises at least 0.01%w/w lignin, such as in the range of 0.01-10w/w% lignin, or in particular in the range of 0.5-10 w/w%, or in the range of 1-9 w/w%, or in the range of 2-8 w/w%, or in the range of 2-7w/w%.

In principle any source of lignin may be used in the composition. Lignin could be used in a solid of fluid form dependent of the kind of animal feed, fodder of food supplement manufactured.

Lignin could be used in the composition in a solid form, in particular as a granulate or powder.

Lignin could be used in the composition in a fluid form, in particular as an extract.

Processes for extracting lignin are well known in prior art. Wood treated with organic solvents such as alcohols to separate the wood's lignin, hemicellulose, sugar and cellulose fractions are for example known from US 1.856.567, US 3.585.104, WO98/27830, US 4.100.016 and WO92/13849 all of which are hereby incorporated by reference.

One method of extracting lignin is to subject the plant material containing lignin to autohydrolysis, wash with water and then subject it to an alkaline treatment. The resulting lignin extract could be precipitated with acid, centrifuged and will typical have a lignin content of more than 90 w/w%. The contaminants will mainly be ash, sugar and some cellulose. The extraxt could furthermore be dried followed by crushing or milling to obtain a granulate or powder with a desired particle size, e.g. by sieving.

As mentioned above there are several types of lignin having somewhat different properties, for example hydrolytic lignin, kraft lignin or organosolv lignin. Sources of hydrolytic lignin are softwood, hardwood, cereal straw and sugarcane bagasse where kraft lignin is derived from softwood and hard wood. Sources of organosolv lignin are a mixture of marple, birch and poplar wood.

An aspect of the composition of the present invention is to use lignin provided from bioethanol production.

In production of bioethanol a fibre-rich plant material which contains a complex mixture of cellulose, hemicellulose bonded by lignin is subjected to hydrolysis and sugar fermentation processes. First lignin in the fibre-rich plant material is broken down by fermentation such that cellulose and hemicellulose can be degraded to monosaccharides/sugar by enzymes or dilute acids. The sugar is then fermented into ethanol. It is this waste product of lignin which can be used in the composition of the present invention.

Examples of suitable sources of plant material which may be used in the bioethanol production include but are not limited to crops grown specifically for energy use and include corn, maize and wheat crops, waste straw, willow and popular trees, sawdust, reed canary grass, cord grasses, jerusalem artichoke, myscanthus and sorghum plants.

Without being bound to any theory the inventors of the present invention believes that a composition comprising lignin in combination with at least one of the compounds selected from the group of bromelain, papain, tannin, carvacrol, thymol, alliin, allicin, fenugreek seed, egg, poppy, poppy seeds, humic acid, roots, kaolin, catechu, cellulase, flavonoid and isphagula husk has a beneficial effect on the gastrointestinal tract and thus may alleviate diarrhoea.

It is believed that the present composition is adequate to support an increased weight gain and survival of animals such as piglets by having an antidiarrhoeal effect.

Lignin is produced as a waste-product from a number of different industrial processes in which a fibre rich material is used. Examples of such industrial processes include but are not limited to production of paper. It is contemplated that the lignin which is produced as a waste product from any of these processes may be used in the present invention.

The compound selected from the group consisting of bromelain, papain, tannin, carvacrol, thymol, alliin, allicin, fenugreek seed, egg, poppy, poppy seeds, humic acid, roots, kaolin, catechu, cellulase, flavonoid and isphagula husk could in principle be included in the

present composition in any solid or fluid form, examples thereof include but are not limited to an extract, oil, granulate, or powder.

Bromelain

The inventors of the present invention have found that administration of bromelain to piglets increases weight of these animals faster than control animals which are not administered bromelain.

Bromelain, which can be found in pineapple, is by the present inventors believed to contain substances that aid digestion and may help to control diarrhoea in animals.

The composition according to the present invention may comprise bromelain in any form such as a pure form, granulate, powder or as an extract of pineapple, small pieces of pineapple, or as crushed or mashed pineapple.

In an aspect of the present invention the composition comprises lignin and bromelain.

In an embodiment of the invention the composition comprises bromelain in a range of 0.01-5w/w%, such as 0.05-2.5w/w%, such as 0.1-2w/w%, or such as 0.1-1.5w/w% or such as 0.5w/w%.

Papain

Papain is a cysteine protease which belongs to EC 3.4.22.2 and which can be found in papaya.

The composition according to the present invention may comprise papain in any form such as a pure form, granulate, powder or as an extract of papaya, small pieces of papaya, or as crushed or mashed papaya.

In an aspect of the present invention the composition comprises lignin and papain.

In an embodiment of the invention the composition comprises papain in a range of 0.01-5w/w%, such as 0.05-2.5w/w%, such as 0.1-2w/w%, or such as 0.1-1.5w/w% or such as 0.5w/w%.

Tannin

Tannins are astringent, bitter-tasting plant polyphenols that bind and precipitate proteins. The term is applied to any large polyphenolic compound containing sufficient hydroxyls and

other suitable groups (such as carboxyls) to form strong complexes with proteins and other macromolecules. Tannins have molecular weights ranging from 500 to over 20,000.

Tannins are usually divided into hydrolyzable tannins and condensed tannins (proanthocyanidins).

It is foreseen that any source of tannin may be used in the present invention.

One example of a useful source of tannin is sweet chestnut wood, such as the commercially available product Globatan.

Globatan is provided from a tannin extract which comes from sweet Chestnut wood. The inventors of the present composition believe that Globatan has an antidiarrhoeal effect and thus attribute to an increased weight gain and decreased mortality of e.g. newborn animals.

Globatan can be provided from a natural source or synthetically prepared. Furthermore Globatan can be mixed to the present composition in any solid or fluid form such as a tannin extract, an extract of sweet Chestnut Wood, a powder or granulate of sweet Chestnut Wood.

In an aspect of the present invention the composition comprises lignin and tannin.

In an embodiment of the invention the composition comprises tannin in a range of 0.1-10w/w%, such as 0.5-9w/w%, such as 1-8w/w%, or such as 2-7w/w% or such as 5w/w%.

Carvacrol

Carvacrol or isopropyl-o-cresol is constituent of the etheric oil of oregano, thyme, Pepperworth, St John's wort, or wild bergamot.

Useful sources of carvacrol include but are not limited to oil, extract, powder or granulate of oregano, thyme, Pepperworth, St John's wort, or wild Bergamot or synthetically prepared carvacrol can be used.

The inventors of the present invention have found that administration of an oregano extract to piglets increases weight of these animals faster than control animals which are not administered an oregano extract.

It is believed by the inventors of the present invention that Carvacrol has a beneficial effect on the gastrointestinal tract and thus has an antidiarrhoeal effect.

In an aspect of the present invention the composition comprises lignin and carvacrol.

In an embodiment of the invention the composition comprises carvacrol in a range of 0.01-5 w/w%, e.g. 0. 05-1 w/w% or 0.1- 0.5 w/w% or 0.2-0.4 w/w% or 0.3-0.4 w/w%, such as 0.2 w/w% or 0.3 w/w% or 0.35 w/w% or 0.4 w/w%.

Thymol

Thymol is a constituent of the etheric oil of thyme and oregano. Thymol may be present in the composition according to the invention as for example an oil or extract of thyme or oregano, leaves of thyme or oregano or leaves grounded to a powder or granulate with a desired particle size.

In another embodiment thymol may be provided from ajwain fruit such as ajwain seed. Thymol may be mixed to the present composition as for example an extract or oil of Ajwain seed or as crushed or ground seeds of ajwain such as a powder of ajwain seed.

The inventors of the present invention have found that administration of ajwain seeds to piglets increases weight of these animals faster than control animals which are not administered ajwain seeds.
The inventors of the present invention believe that thymol has a beneficial effect on the gastrointestinal tract and thus have an antidiarrhoeal effect.

In an aspect of the present invention the composition comprises lignin and a thymol source.

In an embodiment of the invention the composition comprises thymol in a range of 0.01-5 w/w%, e.g. 0. 05-1 w/w% or 0.1- 0.5 w/w% or 0.2-0.4 w/w% or 0.3-0.4 w/w%, such as 0.2 w/w% or 0.3 w/w% or 0.35 w/w% or 0.4 w/w%.

Alliin/allicin

Both alliin and allicin are active substances from garlic and can in principle be administered to the present composition in any solid or fluid form such as an extract of alliin and/or a garlic extract, chopped or crushed garlic or a granulate or powder of garlic.

The inventors of the present invention believe that alliin and/or allicin have antidiarrhoeal effects and thus are beneficial for the health, weight gain and survival of animals.

In an aspect of the present invention the composition comprises lignin and alliin and/or allicin.

In an embodiment of the invention the composition comprises alliin and/or allicin in a range of 0.0001-0.05 w/w%, such as 0.0005-0.01 w/w% or 0.001-0.005 w/w% or 0.002-0.004 w/w% or 0.0025-0.004 w/w% or 0.002-0.0035 w/w%, e.g. 0.002 w/w% or 0.003 w/w% or 0.004 w/w%.

Fenugreek seed

Fenugreek seed can be administered to the present composition in any solid or fluid form, in particular but not limited to an extract or an oil of fenugreek seed, a granulate or a powder with a particular particle size.

The inventors of the present invention have found that administration of fenugreek seeds to piglets increases weight of these animals faster than control animals which are not administered fenugreek seeds.

The inventors of the present invention believe that fenugreek seed has an improving effect on the gastrointestinal tract, such that diarrhoea is alleviated in animals and the weight gain is increased.

In an aspect of the present invention the composition comprises at least lignin and fenugreek seed.

In an embodiment of the invention the fenugreek is present in the composition in a range of 0.1-20%w/w, such as in the range of 1-15%w/w, or such as in the range of 2-12%w/w, or such as in the range 0f 4-12%w/w, or such as 8.5%w/w.

Egg

The composition according to the invention may comprise egg such as whole egg powder which is egg prepared as a powder. In principle whole egg could be present in the composition in fluid state.

The inventors of the present invention have found that administration of whole eggs to piglets increases weight of these animals faster than control animals which are not administered whole eggs.

Whole egg is by the inventors believed to have an antidiarrhoeal effect on animals.

Whole egg is in general a good source of proteins and fatty acids with a 16-18 carbon atoms. The egg yolk itself is a good source of proteins and fatty acids such as palmitic acid and stearic acid, while the egg white comprises several amino acids which are important for a healthy diet. Examples of commercially available whole egg powder include but are not limited to WAF Whole Egg Powder from Belovo and Egg Powder from Schaffelaarbos.

In an aspect of the present invention the composition comprises lignin and egg.

In an embodiment of the invention egg is present in a range of 0.1-20%w/w, such as in the range of 1-15%w/w, or such as in the range of 2-12%w/w, or such as in the range 0f 4-12%w/w, or such as 8.5%w/w.

Poppy/poppy seed

The poppy (*Papaver*) is a member of the poppy family, botanical name *Papaveraceae*. The poppy comprises round seed capsules which contain tiny black seeds (poppy seeds). The poppy seed contains 40 to 50% of fatty oil which can be obtained by cold pressing the seeds. The poppy seed oil is rich in unsaturated fatty acids such as linoleic acid (60%), oleic acid (30%), linolenic acid (3%) and less than 10% saturated fats.

The poppy and/or poppy seed present in the composition according to the invention can in principle be derived from all members of the poppy family such as *Papaver rhoeus L.*, known as corn or field poppy, *Papaver somniferum L.*, *Papaver orientale L.*, formerly *Papaver bracteatum Lindl.*, known as morphine-free alkaloid poppy.

The inventors believe that poppy and/or poppy seed has an antidiarrhoeal effect in the gastrointestinal tract.

The present composition can in theory comprise any form of Poppy seed such as but not limited to whole poppy seed, an oil of the seed, an extract, a powder or granulate.

In an aspect of the present invention the composition comprises lignin and poppy and/or poppy seed.

In an embodiment of the invention poppy seed is present in the composition in an amount of 0.05-10 w/w%, such as 0.01-5 w/w% or 0.1-5 w/w% or 0.2-2.5 w/w% or 0.4-1 w/w% or 0.5-1 w/w% or 0.6-1 w/w% or 0.7-1 w/w% or 0.8-0.9 w/w%, e.g. 0.7 w/w% or 0.8 w/w% or 0.85 w/w% or 0.9 w/w% or 0.95 w/w%.

Humic acid

Humic acids are a complex mixture of partially "decomposed" and otherwise transformed organic materials and is one of the major components of humic substances

Humic acid is for example present in sphagnum which is often classified as a fodder to pigs but which also gives pigs the opportunity to root or grub in it.

Examples of sphagnum materials comprising humic acid which are commercially available include but are not limited to Fibremin from Vitfoss and Promax from Humatech, AZ/TX, USA.

The inventors of the present invention have found that administration of humic acid to piglets increases weight of these animals faster than control animals which are not administered humic acid.

Humic acid is believed by the inventors to have an antidiarrhoeal effect and can be comprised in the composition in the range of 0.5-50 w/w%, such as 1-25 w/w% or 1-20 w/w% or 1-15 w/w% or 2-15 w/w% or 4-15 w/w% or 4-12 w/w% or 4-10 w/w% or 5-10 w/w% or 6-9 w/w% or 6-8 w/w%, e.g. 6 w/w%, 7 w/w% or 8 w/w%.

Roots

The present invention may comprise a root which in principle may be any root. Examples of roots include but are not limited to beetroot and sugar root or turnip, in particular swede turnip, yellow Bortfelder turnip and early garden.

It is believed by the inventors that roots have an antidiarrhoeal effect on the gastrointestinal tract.

The root can be present in the composition in any solid or fluid form such as in solid state as chopped or crushed root or as a powder or granulate with a desired particle size, or in fluid state as an extract of the root.

In an aspect of the invention the composition comprises lignin in combination with a root.

In an embodiment of the invention root is present in the composition in an amount of 0.1-99.9 w/w%. The amount of roots in the composition of the present invention may vary according to which other components are present in the composition. Besides, roots may be used in the composition as a filler.

Kaolin

Kaolin is a naturally occurring clay rich in the mineral kaolinite having the chemical composition $Al_2Si_2O_5(OH)_4$.

Kaolin may be used in solid or fluid form such as a powder, semi-dry noodle, paste, or liquid slurry.

In an aspect of the invention the composition comprises lignin and kaolin.

In an embodiment of the invention kaolin is present in the composition in the range of 0.5-20 w/w%, such as 1-20 w/w% or 5-20 w/w% or 10-20 w/w% or 1-15 w/w% or 1-12 w/w% or 1-10 w/w% or 2-15 w/w% or 3-15 w/w% or 5-15 w/w% or 5-10 w/w.

Catechu

Catechu (also known as Cutch, or Cashoo) is an extract obtained from several plants. Examples of catechu sources include but are not limited to the two species of *Acacia catechu* and *Acacia suma*, known as dark catechu and the *Catechu pallidum*, *Uncaria gambir* and Uncaria acida known as pale catechu. Another source of catechu is for example the fruits of areca or betel palm, *Areca catechu*.

Catechu may in principle be present in the composition according to the invention in any solid or fluid state such as but not limited to a powder, oil or extract.

Catechu may be dissolved in heated water such as boiling water, alcohol, acetic acid and strong caustic alkali. For example the extract of catechu may be produced by boiling the wood in water and evaporating the resulting brew.

Catechu may in principle be used in any solid or fluid form such as extracts, oils, powder, granulate, etc.

In an aspect of the invention the composition comprises lignin and catechu.

Cellulase

Cellulases or cellulolytic enzymes are enzymes involved in hydrolysis of cellulose. In the hydrolysis of native cellulose it is known that there are three major types of cellulase enzymes involved, namely cellobiohydrolase (1,4-beta-D-glucan cellobiohydrolase, EC 3.2.1.91), endo-beta-1,4-glucanase (endo-1,4-beta-D-glucan 4-glucanohydrolase, EC 3.2.1.4) and beta-glucosidase (EC 3.2.1.21). In the context of the present invention the term "EC" (Enzyme Class) refers to the internationally recognized enzyme classification

system, Recommendations of the Nomenclature Committee of the International Union of Biochemistry and Molecular Biology, Academic Press, Inc.

Cellulases are synthesized by a large number of microorganisms which include fungi, actinomycetes, myxobacteria and true bacteria but also by plants. Especially endoglucanases of a wide variety of specificities have been identified.

In principle any source of cellulase may be used in the present invention, e.g. the cellulase may be obtained from a microorganism which naturally expresses the enzyme, or a recombinant expressed cellulase or a synthetic cellulase.

The cellulase may in principle be used in any solid or fluid form such as a powder or a suspension.

In an aspect of the invention the composition comprises lignin and cellulase.

In an embodiment of the invention cellulase is present in the composition in an amount of in a range of 0.01-5w/w%, such as 0.05-2.5w/w%, such as 0.1-2w/w%, or such as 0.1-1.5w/w% or such as 0.5w/w%.

Flavonoids

The term flavonoid refers to a class of plant secondary metabolites based around a phenylbenzopyrone structure. Flavonoids are also commonly referred to as bioflavonoids in these terms are equivalent and interchangeable, since flavonoids are biological in origin.

So far the following subclasses of flavonoids have been identified: flavonols, flavones, flavanones, flavan-3-ols and anthocyanidins. The content of flavonoids differ between individual plants both with regard to the identity of the particular flavonoids, the ratio between different flavonoids for those plants where more than one flavonoid is present and the amount of flavonoid present.

Examples of the content of flavonoids in selected foods may e.g. be found in USDA Database for the Flavonoid Content of Selected Foods issued by the U.S. Department of Agriculture in March 2003.

It is within the scope of the present invention to use any subclass of flavonoids or combination of flavonoids. It is furthermore within the scope of the present invention to use any source of flavonoids.

In one embodiment the flavonoid of the present invention is a flavonol, such as quercetin, kaempferol, myricetin or isorhamnetin.

In another embodiment the source of flavonoid in the present invention is cocoa which comprises the flavonol quercetin.

The inventors of the present invention have found that administration of cocoa powder to piglets increases weight of these animals faster than control animals which are not administered cocoa powder.

In an embodiment of the invention flavonoid is present in the composition in an amount of in a range of 0.25-50w/w%, such as 1-40w/w%, such as 3-35w/w%, or such as 5-30w/w% or such as 5-25w/w%, such as 10-35w/w%, or such as 15-30w/w% or such as 10-20w/w%, or such as 15-35w/w% or such as 20-30w/w%.

Isphagula Husk

Isphagula husk is a fibrous material which is also termed psyllium (husk) and is described in WO2004/043451 which is hereby incorporated for reference. The isphagula husk contained fibrous material comprised in the present composition may be the so-called mucopolysaccharide originating from Plantago ovata.

Since isphagula husk is an intumescent, water absorbing agent which seems to provide a non-specific binding between the mucopolysaccharides and the cell wall it is believed by the inventors that psyllium fibres can be used successfully for the treatment of both diarrhoea and obstipation.

The psyllium fibres present in the composition may for example be dried seed coats of plantago ovata, crushed seeds, ground seeds, a granulate or powder. Thus the psyllium fibres are usually used as a pulverized preparation which can be used directly in the composition or dispersed in a liquid such as water.

In an aspect of the invention the composition comprises lignin in combination with at least isphagula husk.

In an embodiment of the invention isphagula husk is present in the composition in an amount of 0.1-99.9 w/w%. The amount of isphagula husk in the composition of the present invention may vary according to which other components are present in the composition. Besides, isphagula husk may be used in the composition as a filler, thickener or bulking agent.

Other components

In an aspect of the invention the composition may further comprise one or more components selected from the group of amino acid, electrolyte, protein, fat, carbohydrate, peptide, thickener, emulsifier, filler, vitamin, preservative, mineral, colouring, and flavouring.

The content of that other component in the composition is dependent of which product the composition is used for. For example when the composition is used for making an animal feed or fodder the composition will generally further comprise a source of protein, carbohydrate, and/or fat because these three groups are all relevant for the intake of energy by an animal or human being. If the composition is used as a feed additive or feed supplement it may also comprise protein, carbohydrate or fats.

Protein, carbohydrate and fat are all generalised terms covering within each group structurally different proteins, including e.g. enzymes, carbohydrates and fats.
The present compositions may further comprise a number of other components which do not belong to any of these three classes or groups.

In an embodiment of the invention the composition is a food, feed or fodder, and it further comprise protein, fat and/or carbohydrate. The content of the protein in the composition may be in the range of 25-90 w/w% proteins, such as in the range of 30-80 w/w%, or in the range of 30-70 w/w%, or in the range of 30-60 w/w%, or in the range of 40-80 w/w%, or in the range of 40-70 w/w%, or in the range of 40-60 w/w%, or in the range of 35-80 w/w%, or in the range of 35-70 w/w%, or in the range of 35-60 w/w%, or in the range of 45-55 w/w%.

The content of fat in the food, feed or fodder composition may be in the range of 5-50 w/w% fats, such as in the range of 5-45 w/w%, or in the range of 10-45 w/w%, or in the range of 10-40 w/w%, or in the range of 15-35 w/w%, or in the range of 20-30 w/w%, or in the range of 17.5-27.5 w/w%, or in the range of 10-30 w/w%, or in the range of 20-50 w/w%, or in the range of 20-40 w/w%.

The content of carbohydrate in the food, feed or fodder composition may be in the range of 3-40 w/w% carbohydrates, such as in the range of 5-35 w/w%, or in the range of 5-30 w/w%, or in the range of 5-25 w/w%, or in the range of 5-20 w/w%, or in the range of 5-15 w/w%, or in the range of 10-35 w/w%, or in the range of 10-30 w/w%, or in the range of 10-20 w/w%, or in the range of 10-15 w/w%. The carbohydrate is defined as being a simple sugar such as a monosaccharide, preferably glucose, or a disaccharide such as

sucrose. In an aspect of the invention the carbohydrate is lactose. Lactose is known as milk sugar and is especially useful for young animals as it is easily metabolised in contrast to other carbohydrates which require degradation or modification by enzymes which are not yet active in young animals. Whey may be used as a source of lactose.

In an embodiment the composition of the present invention may have a content of proteins and fats, or proteins and carbohydrates, or fats and carbohydrates, or proteins, fats and carbohydrates as described above.

The choice of the particular proteins, fats and carbohydrates in the composition may vary, in particular because different components may be used to prepare the composition of the present invention.

It is not only the amount of protein in the composition which is of relevance but also the amino acid composition may be highly relevant. If for example the composition of the present invention is to be used as a feed or food composition such as to feed newborn piglets it may be advantageous to include sources of amino acids, especially essential amino acids as known to a person skilled in the art, and especially sources of glutamine, glutamate, proline, methionine and phenylalanine. However, the composition according to the invention can in principle comprise any amino acid. Thus the composition may comprise one or more amino acids selected from the group consisting of all known amino acids, preferably at least one selected from the group of glutamine, arginine, lysine, histidine, phenylalanine, tyrosine, leucine, isoleucine, methionine, valine, alanine, glycine, praline, glutamic acid, serine, threonine, aspartic acid, tryptophan, cystine,
Examples of suitable sources of amino acids include but are not limited to whole egg, wheat, soy protein and/or colostrum of animals.

In an embodiment of the invention the amino acid is present in the composition as a linkage of amino acids, such as a peptide.

In a further aspect of the invention the composition comprises one or more electrolytes. An animal having diarrhoea has a risk of losing salts. When administrating a composition comprising electrolytes some of the salts lost by diarrhoea will be replaced and the balance of dehydration and rehydration will be brought into order.

Electrolytes suitable for use in the present composition include but are not limited to magnesium oxide, magnesium carbonate hydroxide, magnesium hydroxide, magnesium silicate, calcium silicate, calcium carbonate, sodium chloride, potassium chloride, sodium hydrogen carbonate, potassium hydrogen carbonate, aluminium phosphate, aluminium

hydroxide, citric acid, sodium citrate, trisodium citrate dehydrate, potassium citrate and phosphates such as sodium phosphate and potassium phosphate.

In a further aspect of the invention the composition comprises one or more thickener. A suitable thickener for use in the present invention include but are not limited to guar gum, alginic acid or its salts, agar, carrageenan, philippine eucheuma seaweed, carob (locust) bean gum, traganth, gum arabic, xanthan gum, karaya gum, tara gum, gellan gum, konjac gum, pectin, cellulose, inulin and psyllium. The inclusion of a thickener in the composition of the present invention has the advantage that it increases the viscosity of the composition. This may be an advantage if the composition is to be used as a food or feed as it may improve the mouthfeel of the composition and may hinder precipitation of heavy and/or insoluble/undissolved components of the solution. In one embodiment of the invention the composition is a viscous liquid which is injected directly into the mouth of a newborn animal since the newborn animal still suckles on a nursing animal. In this embodiment a thickener is an advantage as to give the liquid composition a desired viscosity.

Besides a thickener the composition may comprise one or more emulsifiers. Suitable emulsifiers which may be used include but are not limited to polyoxyethylene (polysorbate) and its derivatives, ammonium phosphatides, polyethylene glycol and its derivatives, beta-cyclodextrin, fatty acid salts and derivatives, mono- and diglycerides of fatty acids and derivatives thereof, propylene glycol and derivatives, polyglycerol and its derivatives, salts of lactylate, stearyl tartrate and derivatives of sorbitol.

The present composition may comprise one or more fillers. Suitable fillers include but are not limited to a fibrous bran material, starch, and wheat flour.

The composition may comprise one or more vitamins. Examples of suitable vitamins include but are not limited to vitamin A, vitamin B, vitamin C, vitamin D and vitamin E, vitamin K.

In an aspect of the invention the present composition may comprise a preservative so that the storage time of the composition may be prolonged. If the composition is to be used as an animal food or animal food supplement said preservative may in particular be a preservative which is non-toxic to animals. Furthermore the preservative may in particular be a preservative which protects the composition against bacterial and fungal growth for a period of at least one year. Examples of suitable preservatives include but are not limited to sorbic acid and its salts, propionic acid and its salts, benzoic acid and its salts and derivatives thereof, sulphite and its salts, diphenyl, o-phenylphenol and its salts, nisin,

natamycin, hexamethylenetetramine, dimethyldicarbonate, nitrite and its salts, nitrate and its salts, acetic acid and its salts, lactic acid, boric acid and its salts, carbon dioxide, malic acid, fumaric acid, calcium propionate, potassium sorbate. It is also foreseen that combinations of one or more of these compounds may be used in the composition of the present invention.

The composition may comprise one or more minerals. Suitable minerals include but are not limited to iron, copper, manganese and zinc. These minerals are often bound in complexes and reference to the minerals is intended to include such complexes.

The composition may comprise a colouring agent which in principle can be any known colouring agent.

The composition may comprise a flavouring agent which in principle can be any known flavouring agent.

Composition

As described above the present invention relates to a composition comprising lignin and at least one compound selected from the group consisting of bromelain, papain, tannin, carvacrol, thymol, alliin, allicin, fenugreek seed, egg, poppy, poppy seeds, humic acid, roots, kaolin, catechu, cellulase, flavonoid and isphagula husk.

The composition of the present invention may in principle be in any form; e.g. liquid or solid form, such as powder, granulate, gel, paste, or fluid. The choice of form may depend on the components of the composition but it may also depend on the mode of administration of the compound.

As the components which may be present in the composition are different the amount of a component used will vary and may affect the amount of another component. For example are some of the components active substances derived from plant material such as a herb, and is only required in a small amount, while other components are food ingredients as such, such as whole egg, ajwain and fenugreek, and they will typically be present in a larger amount. Thus the ratio between lignin and one or more of the other components will vary according to which component(s) are used.

Furthermore the amount of a component present in the composition will vary according to how many other components are added to the composition and the nature of those components.

The composition of the present invention may be used a either a feed or a feed supplement wherein the composition as a feed supplement may consist of lignin and one or more of the components selected from the group of bromelain, papain, tannin, carvacrol, thymol, alliin, allicin, fenugreek seed, egg, poppy, poppy seeds, humic acid, roots, kaolin, catechu, cellulase, flavonoid and isphagula husk, such that the total amount of lignin and the other component is 100 w/w%

Another embodiment of the composition is as a feed supplement comprising other components such as any of those mentioned above.

In still another embodiment the composition is used as a feed such as an animal feed, comprising further components which are typically used in a animal diet such as amino acid, electrolyte, protein, fat, carbohydrate, thickener, emulsifier, filler, vitamin, preservative, mineral, colouring, and flavouring.

In an embodiment of the invention lignin may be present in a feed supplement in an amount in the range of 0.01-30w/w%.

In another embodiment of the invention lignin may be present in a food or feed in an amount in the range of 0.01-10w/w%.

The composition used a food- or feed supplement feed or food may comprise components which in particular may constitute between 0.5-20w/w% of the composition. Examples of such components may be any of the above mentioned.

0.1-5w/w% vitamins,
0.1-5w/w% electrolytes,
0.5-5 w/w% thickeners,
0.01-3 w/w% emulsifier,
0.01-3w/w% filler,
0.5-10 w/w% preservatives,
0.01-3 w/w% minerals,
0.0004-4 w/w% colouring,
0.0004-4 w/w% flavour.

Examples of suitable sources of lignin, bromelain, papain, tannin, carvacrol, thymol, alliin, allicin, kaolin, catechu, cellulose, flavonoid and isphagula husk which may be used in the composition may in particular be any of the above mentioned.

Furthermore examples of suitable egg, roots, amino acid, electrolyte, protein, fat, carbohydrate, thickener, emulsifier, filler, vitamin, preservative, mineral, colouring, and flavouring etc. which may be used in the composition may in particular be any of the previously mentioned.

Method of preparing the composition

A further aspect of the invention relates to a method of preparing the present composition comprising mixing lignin with one or more of the compounds selected from the group consisting of bromelain, papain, tannin, carvacrol, thymol, alliin, allicin, fenugreek seed, egg, poppy, poppy seeds, humic acid, roots, kaolin, catechu, cellulase, flavonoid and isphagula husk. Additionally, one or more components selected from the group of amino acid, electrolyte, protein, fat, carbohydrate, thickener, emulsifier, filler, vitamin, preservative, mineral, colouring, and flavouring can be mixed in the composition.

In principle the components of the composition may be mixed in any order.

The components of the composition can be either solid or in liquid state dependent of which kind of product is prepared such as described above. Thus the components may be extracts, oils, solutions, powders, granulates or other forms, and for most purposes is the mixing of a liquid and solid (powder) component not a problem. A factor which may affect how thoroughly the components need to be mixed is the ratio between hydrophilic and lipophilic components in the composition as it is well known that these two types of components do not mix easily. Furthermore whether a component has hydrophilic or lipophilic characteristica may also affect in what order it is advantageously to mixing them.

The mixing of the components may be by using any conventionally known apparatus for mixing and in general a manual mixing of the components may be enough.
In an embodiment a component which are powders or granulates are mixed with water and different oils such as oils of herbs. The powder-solution is then mixed thoroughly with the oil e.g. together with an emulsifier. The mixing may be manually or mechanically. In another embodiment powders are added directly to an oil or extract of a plant material and then mixed thoroughly. Whether a powder is dissolved in an aqueous solution or an oil depends on the hydrophilic or lipophilic characteristic of the powdered component.

In another embodiment of the invention the composition may be prepared by spray drying. The fluid components of the present invention are first mixed with one or more soluble sugars and/or salts. This mixture is then sprayed onto a mixture of granulates or powders of one or more of the components comprised in the present invention and at the same

time blown with hot air to dry the composition. A Filter mat Dryer may be used for the spray drying.

In still another embodiment a Fluid Bed dryer may be used for drying a mixture of the dry components pasted onto a mixture of the fluid components.

Use of the composition

The inventors of the present invention believe that the composition according to present invention increases weight gain of animals or humans and without being bound by any theory that this may be caused by the composition having beneficial effects on the gastrointestinal tract such as the jejunal intestine and thus can prevent and/or treat animals having diarrhoea. The composition may be used to feed an animal. Examples of such animals which may be fed with the composition include but are not limited to animals such as pigs, cattle, sheep, goats, horses, chickens, turkeys, pigeons, camels, llamas, dogs and cats.

In one aspect of the invention the composition is used to make an animal feed or fodder. The composition then comprises components which are usually used in an animal diet as described above. A feed or fodder will normally comprise a source of fat, protein, carbohydrate, and different nutrients such as minerals and vitamins. The components are mixed and bonded together with an emulsifier, filler and/or pelletizing agent to produce pellets of animal fodder. In principle the animal feed or fodder can be in any form such as pellets and granulate. In an embodiment of the invention the animal feed or fodder is in a viscous liquid form.

In another aspect of the invention the composition is used as a food supplement which is defined not to be a part of an animal feed or fodder but is a supplement which either may be sprinkled onto an animal feed or fodder. The composition may particular be used as a supplement if it is discovered that one or more animals of a herd have diarrhoea and/or if the animal is not gaining enough weight. Then the composition can be administrated to the feed or fodder for a given period until the diarrhoea has stopped and/or has gained enough weight. A new born animal, such as piglet which is still sucking on the nursing sow, will yet not be able to eat ordinary feed or fodder. Thus an embodiment of the invention is a food supplement in a liquid form which can be injected directly into the mouth of the new born animal. The injection of the composition into the mouth of a new born animal can e.g. be by using a syringe or a feeding bottle.

In an embodiment of the present invention the composition is used for the manufacturing of a medicament.

In a further embodiment the medicament may be for treating diarrhoea.

In a further embodiment the medicament may be for increasing the weight.

In an embodiment the composition according to the invention may be administrated to an animal in the range of from 1-3000 mg/kg bodyweight/day of treatment, such as in the range of 3-2000 mg/kg bodyweight/ day of treatment, such as 5-1500 mg/kg bodyweight/ day of treatment, such as 7-1000 mg/kg bodyweight/ day of treatment, such as 10-500 mg/kg bodyweight/ day of treatment, such as 10-300 mg/kg bodyweight/ day of treatment, such as 10-100 mg/kg bodyweight/ day of treatment, such as 20-100 mg/kg bodyweight/ day of treatment. As discussed above the composition can be administrated to the animal directly in the animal feed or fodder or the composition can be administrated to the animal as a feed supplement either sprinkled onto a feed or fodder or injected into the mouth of the animal. If an animal is having diarrhoea caused by a gastrointestinal disorder the animal will typically be given a diet (feed, fodder or supplement) comprising the composition 2-3 times a day for 3-5 days. However the number of treatments per day and period of time may vary according to the degree of disease.

A further embodiment of the invention relates to a method of treating diarrhoea in animals or humans comprising administration of a composition according to the present invention as described above.

A further embodiment of the invention relates to a method of treating underweight in animals or humans comprising administration of a composition according to the present invention as described above.

It should be noted that embodiments and features described in the context of one of the aspects of the present invention also apply to the other aspects of the invention.

All patent and non-patent references cited in the present application are hereby incorporated for reference in their entirety.

The invention will now be described in further details in the following non-limiting examples.

Examples

Example 1

Studies with a total of 240 piglets per compound were conducted to test the effect of bromelain, fenugreek seeds, cocoa powder, oregano leaves and ajwain seeds, Humic acid, oregano extract, and whole egg powder on the piglets' weight gain.

The piglets were divided into two groups of 120 piglets. One group received regular feed supplemented with a standard antidiarrhoeal product, hereafter referred to as the control group, and the other group received regular feed supplemented with a standard antidiarrhoeal product as well as one of the following compounds:

Group A: 8.5 g bromelain per day per group

Group B: 143 g fenugreek seeds per day per group

Group C: 71 g cocoa powder per day per group

Group D: 60 g oregano leaves per day and 120 g ajwain seeds per day per group

Group E: 120 g humic acid per day per group

Group F: 11 g oregano extract (Ropadiar fra Ropapharm) per day per group

Group G: 143 g whole eggs powder from Schaffelaarbos per day per group

The weight of the piglets was measured at the beginning of the study and then again 14 and 28 days later.

The average weight of the piglets within each group at day 14 and 28 was adjusted for piglets which were cancelled from the study due to e.g. death as it was assumed that such piglets had a low weight and therefore the average weight within the group would increase if they were just left out.

The control group for each of the groups A-G was pooled, such that the groups of 120 piglets each containing a compound as in the groups A to G was compared not only to 120 piglets of a control group but to 7x120 piglets from all the control groups.

The varying weights of the piglets at the beginning of the test were adjusted, such that the real weight gain was calculated.

In addition, an adjustment for different weight rates of piglets was conducted.

On the basis of the measured weight of the piglets, the average weight gain of each of the groups A to G containing an active compound was measured and compared to the measured average weight gain of the pooled control groups.

The calculations of an average weight gain of one of groups A-G compared to the total control group were conducted by the random effect model.

The results are shown in table I as the average weight gain within a group compared to the pooled control group:

Group	Compound	Average weight gain compared to control group (g/week per pig)	Standard error
A	Bromelain	245	92
B	Fenugreek seeds	286	104
C	Cocoa powder	80	92
D	Oregano leaves/ ajwain seeds	96	91
E	Humic acid	155	92
F	Oregano extract	112	92
G	Whole eggs powder	94	92

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Claims

1. A composition comprising lignin and at least one compound selected from the group consisting of bromelain, papain, tannin, carvacrol, thymol, alliin, allicin, fenugreek seed, egg, poppy, poppy seeds, humic acid, roots, kaolin, catechu, cellulase, flavonoid and isphagula husk.

2. The composition according to claim 1 wherein lignin is in a solid or fluid state.

3. The composition according to any of the claims 1-2 which further comprises one or more components selected from the group of amino acid, electrolyte, protein, fat, carbohydrate, thickener, emulsifier, filler, vitamin, preservative, mineral, colouring, and flavouring.

4. The composition according to any of the claims 1-3, wherein the composition is an animal feed supplement.

5. The composition according to claim 4, wherein the composition is in a solid or fluid state.

6. The composition according to claim 4 or 5, wherein lignin is present in the range of 0.01-30w/w%.

7. The composition according to any of the claims 1-3, wherein the composition is an animal feed.

8. The composition according to claim 7, wherein lignin is present in the range of 0.01%-10w/w%.

9. The composition according to claim 1 or 2, wherein the total amount of lignin and the at least one compound selected from the group consisting of bromelain, papain, tannin, carvacrol, thymol, alliin, allicin, fenugreek seed, egg, poppy, poppy seeds, humic acid, roots, kaolin, catechu, cellulase, flavonoid and isphagula husk is 100w/w%.

10. Method to prepare a composition according to any of the claims 1-9 comprising mixing lignin with one or more of the compounds selected from the group consisting of bromelain, papain, tannin, carvacrol, thymol, alliin, allicin, fenugreek seed, egg, poppy, poppy seeds, humic acid, roots, kaolin, catechu, cellulase, flavonoid and isphagula husk, and optionally further components.

11. The composition according to any of the claims 1-9 for the use as a medicament.

12. Use of a composition according to any of the claims 1-9 for the manufacture of a medicament for treating diarrhoea.

13. Use of the composition according to any of the claims 1-9 as food, feed or supplement for humans, pigs, cattle, sheep, goats, horses, chickens, turkeys, pigeons, camels, llamas, dogs and cats.

14. Use of the composition according to any of the claims 1-9, wherein the composition is administrated to a human or an animal in a concentration such that lignin in combination with one or more of the compounds selected from the group of bromelain, tannin, carvacrol, thymol, alliin, allicin, fenugreek seed, egg, poppy, poppy seeds, humic acid, roots, kaolin, catechu, cellulase, flavonoid and isphagula husk is administrated in the range of from 1-3000 mg/kg body weight/day of treatment.

15. A method of treating diarrhoea in animals or humans comprising administration of a composition according to any of the claims 1-9.

INTERNATIONAL SEARCH REPORT

International application No
PCT/DK2007/050154

A. CLASSIFICATION OF SUBJECT MATTER
INV. A23K1/16 A23K1/18 A23K1/12 A23K1/14 A61P1/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A23K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, FSTA, BIOSIS, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE WPI Week 199538 Derwent Publications Ltd., London, GB; AN 1995-291236 XP002464846 & RU 2 028 805 C1 (N CAUCASUS VETERINARY INST) 20 February 1995 (1995-02-20) abstract -----	1-15
X	DATABASE WPI Week 198550 Derwent Publications Ltd., London, GB; AN 1985-315393 XP002464847 & SU 1 159 540 A (VYAIZENEN G N) 7 June 1985 (1985-06-07) abstract ----- -/--	1-15

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 January 2008	28/01/2008

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Rooney, Kevin

INTERNATIONAL SEARCH REPORT

International application No
PCT/DK2007/050154

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 2005, RAMESH, N. ET AL: "Antimicrobial and phytochemical studies on the leaves of Phyllanthus singampattiana (Sebastine & A.N. Henry) Kumari & Chandrabose from India" XP002464840 retrieved from STN Database accession no. 2005:372237 abstract & MEDICINAL CHEMISTRY RESEARCH , 13(6/7), 348-360 CODEN: MCREEB; ISSN: 1054-2523, 2004, -----	1-15
X	US 5 856 313 A (MARCO ANA MARIA REQUEJO [ES] ET AL) 5 January 1999 (1999-01-05) column 4, line 20 - column 5, line 29 claim 1 -----	1-11,13, 14
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INTERNATIONAL SEARCH REPORT

International application No
PCT/DK2007/050154

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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INTERNATIONAL SEARCH REPORT

International application No
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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claims 11 and 15 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the composition.

Continuation of Box II.1

Claims Nos.: -

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK2007/050154

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: –
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/DK2007/050154

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